



## Review

# Psychobiotics as an Intervention in the Treatment of Irritable Bowel Syndrome: A Systematic Review

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**Abstract:** Today's perceived excess of work versus rest and excessive stressful situations are one of the potential factors for an increasing number of gastrointestinal disorders. Although the prevalence of irritable bowel syndrome (IBS) varies widely, it is assumed that up to 15% of the general population may be affected. Symptoms resulting from IBS take the form of pain, including difficulties with bowel movements, bloating, and a feeling of overflowing in the intestines. These symptoms have a negative impact on patients' quality of life, so any possible intervention supported by Evidence-Based Medicine should effectively contribute to their improvement. In the following review, the authors compile the current knowledge based on the findings of researchers from around the world. The topic of probiotic therapy is increasingly discussed in the field of lower gastrointestinal disorders, and thus the authors discover links between probiotic strains and the improvement of health quality in patients with IBS, taking into consideration the ways it affects patients' mental health. As a result, a systematic review was prepared based on 60 items of recent literature, of which more than 80% were published in the last 5 years.

**Keywords:** irritable bowel syndrome; psychobiotics; stress; GI tract



**Citation:** Gwioździk, W.; Helisz, P.; Grajek, M.; Krupa-Kotara, K. Psychobiotics as an Intervention in the Treatment of Irritable Bowel Syndrome: A Systematic Review. *Appl. Microbiol.* **2023**, *3*, 465–475. <https://doi.org/10.3390/applmicrobiol3020032>

Academic Editor: Ian Connerton

Received: 29 March 2023

Revised: 10 May 2023

Accepted: 12 May 2023

Published: 15 May 2023



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## 1. Introduction

Irritable bowel syndrome (IBS) is one of the most common functional disorders of the lower gastrointestinal tract. The prevalence of IBS varies widely, but it is estimated that the disorder affects 7–15% of the general population, with a twofold predominance in women [1,2]. Irritable bowel syndrome manifests as, among other things, abdominal pain, which is caused by changes in bowel function and defecation. There is no doubt that the accompanying symptoms have a negative impact on a patient's quality of life. In addition, research shows that people diagnosed with IBS have a threefold higher predisposition to develop depression and anxiety disorders compared to healthy individuals [2–5]. The brain-gut axis plays an important role in this case, as the disturbed composition of the gut microbiota significantly affects central nervous system function through signaling pathways [4,5]. Nutritional management is a key element in the treatment of irritable bowel syndrome, as it contributes to not only the frequency of symptoms, but also their severity. A diet low in fermented oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs), known as a low-FODMAP diet, has been shown to have a positive effect in patients with the condition, as it is effective in reducing the symptoms of gastrointestinal dysfunction while also being safe for the gut microbiota if used short-term. [6]. A diet low in FODMAPs is carried out in three phases—an initial 2–6 week restriction phase followed

by re-challenges to assess individual tolerance and a long-term individualized maintenance phase [7].

However, the low-FODMAP diet cannot always be used—for example, in the case of eating disorders, the use of an elimination diet could hinder the treatment process for the eating disorder. At the same time, ongoing eating disorders (e.g., binge-eating syndrome) would have made it impossible to carry out an elimination diet properly. [8]. It is worth noting that eating disorders (e.g., anorexia nervosa, bulimia nervosa, binge eating syndrome) are often associated with mood disorders and co-occurring dysfunctions in neurotransmitter pathways, which in themselves may hinder the proper implementation of a low-FODMAP diet due to reduced overall motivation and sense of purpose in changing eating habits [9–11]. As mentioned before, patients with IBS often struggle with depressive or anxiety disorders, so it is therefore reasonable to search for solutions and elements of therapy that will have a positive impact on intestinal symptoms while taking care of the patient's mental health.

The etiology of irritable bowel syndrome is multifactorial, and thus this issue is an ongoing subject of research and analysis to better understand the specifics of this condition, including treatment options, as well as preventive actions. In view of the above, the authors of this paper aimed to compile the most recent scientific reports on psychobiotics, which may be an important element contributing to the alleviation of gastrointestinal symptoms and thus improving the quality of life of people diagnosed with IBS. To achieve this aim, the following research questions were posed:

Q1: Can modulation of the gut microbiota be beneficial in alleviating IBS symptoms for patients in whom stress is a major aggravating factor?

Q2: Are there psychobiotic strains that have been proven to have a positive effect against IBS symptoms?

Q3: What probiotic interventions can be taken in patients with IBS and mood disorders?

## 2. Materials and Methods

### 2.1. Methodology Background

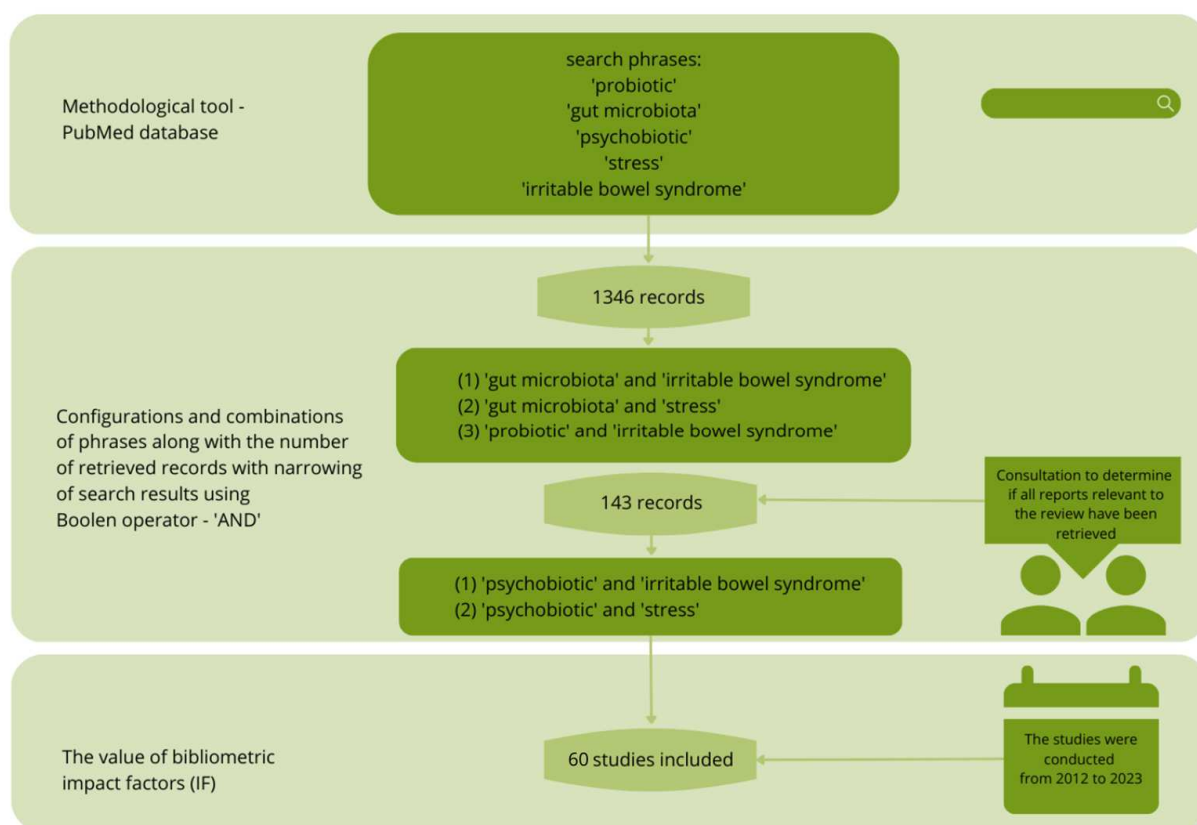
The purpose of this study was to investigate the hypothesis of whether probiotics have a beneficial effect on the health of IBS patients, particularly in terms of psychological impact. Current scientific research leaves no shadow of a doubt that gut microbiota plays a key role in both physical and mental health. It is not without reason that recent reports refer to the microbiota as one of the “organs” of the human being, which encouraged the authors to compile the latest scientific research on the role of psychobiotics in terms of alleviating IBS-related symptoms.

### 2.2. Review Procedure and Search Strategy

The following paper was edited based on good practices that are commonly used in works of this type. The authors of the paper began by defining the research field, and then searched PubMed, and Scopus databases and found scientific publications related to the proposed topic. The literature items were searched by the authors of the paper and a qualified library staff member, using relevant keywords with Boolean operators and their combinations and configurations: probiotics, gut microbiota, psychobiotic, stress, and irritable bowel syndrome (IBS). For this purpose, a methodological tool was used in the form of the databases mentioned above.

### 2.3. Sources Selection

The literature search yielded a large number of records, from which the authors of the paper selected those directly related to the topic of the paper, the number amounted to 1346. In the next step, the records with the highest scientific value were selected according to bibliometric impact factors. In the final literature review, 60 sources were used, representing mainly scientific output from recent years (Figure 1).



**Figure 1.** Methodological scheme.

The GRADE (The Grading of Recommendations Assessment, Development, and Evaluation) system was used to assess the reliability, accuracy, and relevance of the work. One of the main goals of the system is to eliminate confusion resulting from the use of different evaluation methods. As a result, the authors prepared a review paper based on 60 scientific sources from 2012–2023. Particular attention was paid to the most recent scientific studies from the last five years (>80% of the papers) so that the paper takes on the character of a recent summary based on current evidence-based medicine (EBM).

### 3. The potential of Psychobiotics in the Treatment of IBS

#### 3.1. The Brain-Gut Axis in the Context of Gastrointestinal (GI) Tract Ailments

Stress is one of the factors that can both influence the development of irritable bowel syndrome and contribute to the severity of the gastrointestinal symptoms associated with it [12]. Stress refers to the physiological adaptive responses to psychological or actual stress-inducing factors. It is the body's response to threats, or stressors, that exerts an effect on internal balance. When a stressor takes a chronic form, exceeding the body's adaptive capacity, homeostasis is disrupted. A person's current lifestyle, in most cases, correlates positively with chronic stress. Life experiences, for example, illnesses, financial problems, or interpersonal conflicts, are key factors in the persistence of chronic stress [13,14]. Stressors contribute to increased activation of the central sympathetic nervous system and the hypothalamic-pituitary-adrenal (HPA) axis, and thus to increased secretion of cortisol, excess of which can lead to adverse health effects such as obesity, cardiovascular disease, and depressive disorders [15–17].

Stress is also an important predictor of eating behavior. This factor may activate relevant reward (pleasure) center signaling pathways in the brain, which in turn may be associated with increased consumption of unhealthy snacks at the expense of adequate fruit and vegetable intake [15]. An important factor modulating the composition of the gut microbiota is a well-balanced diet based on whole-grain products and large amounts

of vegetables and fruit, which are sources of dietary fiber. In contrast, the ‘Western’ dietary model, which includes a high intake of processed and high-fat products, positively correlates with the development of intestinal dysbiosis, which can cause gastrointestinal symptoms [18–20]. In addition, the presence of gastrointestinal dysbiosis influences the increased incidence of abnormal eating behaviors, which in most cases include irregular food intake as well as food avoidance. This, in turn, leads to food selectivity and worsening intestinal dysbiosis [8]. There is a bidirectional relationship between the host brain and the microbiota, which is regulated via the following pathways: immunological (cytokines), endocrine (cortisol, HPA), neuronal (X nerve, enteric nervous system), and metabolic. In addition, the microbiota can produce various mediators, such as cytokines, short-chain fatty acids, neurons, and neurotransmitters, which show properties that influence the brain, thus affecting its various levels and communication pathways. Any hormonal abnormality (imbalance of the HPA axis) is associated with psychiatric-like disorders [21–24]. Importantly, microorganisms inhabiting the human gastrointestinal tract affect both the development and function of the HPA axis [21,22]. A major role in the above linkage is played by the kidneys and adrenal glands. The adrenal cortex plays an important function in metabolite signaling, as it produces types of steroid hormones such as mineral corticosteroids (e.g., aldosterone), glucocorticosteroids (including cortisol and corticosterone, among others), and androgens. Research reports that all of the above hormones affect the regulation of the gut microbiota in some way. It appears that the adrenal gland produces the same catecholamine hormones as the gut microbiota. In addition, epinephrine and norepinephrine (produced in the adrenal medulla) affect the gut microbiota by increasing the adhesion of gram-negative bacteria to the gut wall. This, in turn, can increase the host’s susceptibility to developing various infections. It is also worth mentioning that epinephrine, norepinephrine, cortisol, and corticosterone are stress hormones whose concentrations increase markedly in situations of high emotional tension, among others [22]. This explains the results of available scientific studies, which show that more than half of IBS patients experience depressive disorders, panic attacks, and anxiety, as well as sleep problems or loss of appetite [12,23].

### 3.2. Composition of the Gut Microbiota in People with IBS in the Context of Mental Disorders

Functional gut disorders are increasingly associated with an abnormal microbiome compared to healthy individuals, and the severity of symptoms may be dependent on specific differences in microbiota composition [25]. This is possibly due to the potential influence of the mucosal adherent microbiota on the host through its ability to interact immunologically and microbiologically [26]. Many intrinsic and extrinsic factors influence the modulation of the human gut microbiota, including gastric acid secretion, gastrointestinal motility, drugs affecting the aforementioned factors, antibiotics, dietary modifications (especially regarding fiber supply), or probiotic supplementation [26]. The brain-gut axis is also important, as one factor in the pathogenesis of IBS is the co-occurrence of neurological disorders. Psychological stress can induce changes in the composition of the gut microbiota, accompanied by increased intestinal permeability and increased expression of pro-inflammatory cytokines. In turn, disturbed microbiota composition may influence the occurrence of anxiety or mood disorders, resulting in a vicious circle effect and exacerbating IBS symptoms [27,28]. Some studies indicate similarities in the microbiomes of people with IBS and those with depression, as indicated by, among others, an abundance of proteobacteria and a scarcity of bifidobacteria [29,30]. An increased abundance of bacteria from the *Enterobacteriaceae*, *Lactobacillaceae*, and *Bacteroides* families was observed in people with irritable bowel syndrome. In contrast, the amount of *Clostridiales*, *Faecalibacterium*, and *Bifidobacterium* was reduced, compared to the microbiome of healthy individuals [30]. A reduction in *Faecalibacterium* and *Bifidobacterium* also characterizes the microbiomes of people suffering from depression [31]. Other sources indicate that in the case of IBS, there is a decrease in *Lactobacillus* and *Bifidobacterium* with an increase in *Escherichia coli*, *Streptococcus*, or *Clostridium* [26]. In the context of the link between the microbiome of IBS sufferers and psychological aspects, it is noteworthy that more than 90% of the body’s serotonin

is synthesized in the gut, mainly by enterochromaffin cells of the intestinal mucosa, but also by bacteria such as *Lactiplantibacillus plantarum* [32,33]. Serotonin is a key neurotransmitter of the gut-brain axis and plays an important role in the pathogenesis and severity of symptoms of both emotional disorders and irritable bowel syndrome by affecting intestinal peristalsis. The production of other neurotransmitters, such as dopamine and norepinephrine, is also possible in the gut [34]. Given that intestinal dysbiosis can affect the biosynthesis, secretion, and reuptake of neurotransmitters, and that mood disorders are a factor in the intensification of IBS symptoms, a therapeutic focus on improving the composition of the intestinal microbiome in such a way as to promote the synthesis of neurotransmitters responsible for mood seems reasonable.

### 3.3. Psychobiotics—A New Class of Probiotics

An adequate composition of the gut microbiota is extremely important for mental health [35]. The gut microbiota performs a variety of important functions. In the eubiosis state, these include the secretion of neurotransmitters such as gamma-aminobutyric acid (GABA), serotonin, or dopamine, the reduction of cortisol synthesis and the synthesis of short-chain fatty acids, which are key to the proper functioning of the intestinal epithelium. In contrast, in a state of dysbiosis, the microbiome is responsible for the production of pro-inflammatory cytokines, the secretion of bacterial toxins, and the removal of harmful metabolites from the diet [36]. Probiotic therapy appears to be effective in improving the composition of the microbiome. According to the FAO/WHO definition, probiotics are live microorganisms that, when administered in an appropriate dose, confer health benefits to the host [37]. In 2020, a new terminology was proposed, according to which probiotic means “a living or non-living bacterial cell (vegetative or spore; intact or disrupted) that is potentially beneficial to the health of the host” [38]. Common properties of probiotics include restoring the balance of the microbiota, improving intestinal epithelial regeneration, increasing the production of short-chain fatty acids, and regulating intestinal transit [39]. A new class among probiotics is psychobiotics. These are bacterial species that can alter brain function by influencing immune function, hormonal signaling or modulating neurotransmitter levels and availability [40]. The main tasks of psychobiotics include protecting the integrity of the intestinal barrier, reducing the synthesis of pro-inflammatory cytokines, producing neuroactive compounds (e.g., GABA), modulating neurotropic factors (e.g., brain-derived neurotrophic factors, or BDNFs), and influencing the synthesis of neurotransmitters [36]. From a practical point of view, psychobiotics are used to reduce stress, reduce depressive symptoms, alleviate anxiety disorders, improve cognitive function, and reduce stress-related gastrointestinal complaints, among others [41]. Given the effects of psychobiotics in reducing symptoms of depression and anxiety disorders, supplementation with psychobiotics is considered a safe option for the prevention of related mental health issues, with a significantly lower risk of side effects (e.g., allergies, addiction, gastrointestinal complaints) compared to psychotropic medications [33]. In turn, the last-mentioned use is particularly relevant to the concept of using psychobiotics in the treatment of functional bowel disorders, which include irritable bowel syndrome. This is because psychobiotics can reduce the intensity of visceral hypersensitivity, which is extremely important in reducing the severity of symptoms of this disorder. This effect is correlated with the concentration of stress hormones such as norepinephrine, corticosterone and adrenaline and is most likely regulated by glucocorticoid receptors [42]. In recent years, the benefits of psychobiotics in relieving stress in people with gastrointestinal complaints associated with mood disorders have been increasingly reported [43,44]. This indicates the high efficacy of probiotics in alleviating gastrointestinal symptoms, not only by regulating the composition of the microbiome per se, but also through its effects of reducing the inflammatory response and emotional regulation.



### 3.4. Practical Use of Psychobiotic Strains in the Treatment of IBS

According to World Gastroenterology Organisation guidelines, appropriately selected probiotic therapy can alleviate symptoms and improve quality of life in patients with irritable bowel syndrome, mainly by reducing bloating and improving bowel rhythm [45]. Strains with documented effects in functional bowel disorders include *Lactiplantibacillus plantarum* 299v (DSM 9843), *Bifidobacterium infantis* 35624, *Lactobacillus rhamnosus* NCIMB 30,174 and *Saccharomyces boulardii* CNCM I-745 [42]. *Lactiplantibacillus plantarum* 299v additionally shows psychobiotic effects, influencing the reduction of anxiety and depressive states [42,46,47]. In turn, psychobiotics that have the potential to reduce stress-induced gastrointestinal complaints include *Lactobacillus helveticus* R0052 and *Bifidobacterium longum* R0175 [42,48,49]. Psychobiotic strains that have the potential to reduce symptoms of irritable bowel syndrome were reviewed below (Table 1).

**Table 1.** Review of selected studies on probiotics with psychobiotic properties that may be beneficial in patients with irritable bowel syndrome.

Probiotic Ingredient	Source	Sample	Effect of Probiotic Therapy
<i>Lactiplantibacillus plantarum</i> 299v	Andersson et al. [47]	A randomised, double-blind controlled trial conducted on 41 students over 14 days.	<i>Lactiplantibacillus plantarum</i> 299v shows the ability to reduce IBS symptoms, but also reduces levels of the stress marker cortisol.
	Krammer et al. [50]	A non-interventional study of 221 patients with IBS using symptom diaries and medical assessments.	During the 12-week treatment period, there was a significant alleviation of global IBS symptoms, including an improvement in mental wellbeing.
	Ducrotté et al. [51]	Double-blind, placebo-controlled, parallel-designed study conducted on 214 participants with diagnosed IBS.	A 4-week supply of the probiotic alleviated IBS symptoms, including abdominal pain and bloating.
	Nordström et al. [52]	Review of in vitro, animal and clinical studies involving the bacterial strain <i>Lactiplantibacillus plantarum</i> 299v.	Supplementation with <i>Lactiplantibacillus plantarum</i> 299v has been shown to have a number of health benefits, including improved intestinal barrier function, reduced intestinal discomfort, improved iron absorption and reduced levels of stress hormones.
<i>Bifidobacterium longum</i> R0175 and <i>Lactobacillus helveticus</i> R0052	Kazemi et al. [43]	Double blind clinical trial conducted with 81 patients with depression for 8 weeks.	An improvement in the Beck Depression Inventory score was observed compared to placebo.
	Arseneault-Breard et al. [49]	Experimental study conducted on 40 rats.	Probiotic therapy with <i>L. helveticus</i> R0052 and <i>B. longum</i> R0175 reduced depressive symptoms and restored intestinal barrier integrity.
<i>Bifidobacterium longum</i> paracasei HA-196	Lewis et al. [48]	Randomised, double-blind, placebo-controlled study involving 285 participants with diagnosed irritable bowel syndrome.	A reduction in bowel frequency was observed in subjects with the diarrhoeal type of IBS. It was concluded that <i>L. paracasei</i> and <i>B. longum</i> may play a clinically relevant role in relieving IBS symptoms.

Table 1. Cont.

Probiotic Ingredient	Source	Sample	Effect of Probiotic Therapy
<i>Lactocaseibacillus paracasei</i> YIT 9029	Kato-Kataoka et al. [53]	A double-blind, placebo-controlled and parallel-group trial conducted on 54 healthy students.	Reduced feelings of stress and stress-induced gastrointestinal complaints were found, as well as reduced cortisol levels.
	Zhang et al. [54]	A randomised, double-blind, placebo-controlled trial conducted on 82 subjects aged 18–60 years with diagnosed depression.	Probiotic supply for nine weeks improved depressive symptoms, reduced the occurrence of constipation and significantly reduced interleukin-6 levels.
<i>Lactobacillus gasseri</i> CP2305	Nishida et al. [55]	Observational study among 31 healthy students aged 18–34 years.	A stress-relieving effect was observed over a 5-week period. In addition, a reduced tendency for diarrhoea was observed among men.
<i>Bifidobacterium longum</i> NCC3001	Pinto-Sanchez et al. [56]	Randomized, double-blind, placebo-controlled study of 44 adults with IBS and diarrhea or a mixed-stool pattern and mild to moderate anxiety and/or depression.	Probiotic intake reduced depressive symptoms and increased the quality of life in IBS patients.
<i>Bifidobacterium infantis</i> 35624	Desbonnet et al. [57]	An experimental study evaluating the potential antidepressant properties of <i>Bifidobacterium infantis</i> in a rat model of depression.	The intake of <i>Bifidobacterium infantis</i> 35,624 resulted in reduced anxiety and stress in young mice.
<i>Bifidobacterium animalis</i> subsp <i>Lactis</i> , <i>Streptococcus thermophiles</i> , <i>Lactobacillus bulgaricus</i> and <i>Lactococcus lactis</i> subsp <i>Lactis</i>	Tillisch et al. [58]	Randomised, controlled, parallel arm designed study conducted in healthy women aged 18–55 years.	A four-week supply of probiotic strains showing efficacy in relieving IBS symptoms affected the activity of brain areas controlling central processing of emotions and sensations.
<i>Lactobacillus rhamnosus</i> NCIMB 30174, <i>Lactobacillus plantarum</i> NCIMB 30173, <i>Lactobacillus acidophilus</i> NCIMB 30175, <i>Enterococcus faecium</i> NCIMB 30176	Moens et al. [59]	Study conducted with an in vitro intestinal model.	Immunomodulatory effect of probiotics: increased production of anti-inflammatory cytokines (IL-6 and IL-10) and decreased production of inflammatory chemokines (MCP-1, CXCL 10 and IL-8).
	Sisson et al. [60]	A single-centre, randomised, double-blind, placebo-controlled trial of adult patients with symptomatic IBS.	Improvement in overall symptom severity in patients with IBS (mainly abdominal pain and abnormal bowel movements).

#### 4. Strengths and Limitations

There is an increasing amount of research in the scientific space addressing therapeutic options in people with irritable bowel syndrome, including the use of probiotics. The impact of stress on the severity of intestinal symptoms in IBS is already fairly well recognized, but there are still few studies further exploring practical therapeutic approaches possible in people whose symptoms are directly related to their psychological state. This research review highlights the potential of psychobiotics in relieving IBS symptoms, combining their effectiveness in improving stress responses and reducing bowel complaints. This review presents current knowledge in this area, and therefore it can be useful for healthcare professionals, identifying new opportunities to supplement IBS therapy. It also points out

the need for a holistic patient approach, taking into account the interdisciplinary nature of the treatment. We have outlined the best-studied psychobiotic strains so far that may be beneficial in improving the quality of life of IBS patients, which is undoubtedly a strength of the study. We also highlighted the need for further human studies into the effects of psychobiotics on markers of stress and gastrointestinal complaints, taking into consideration changes in the composition of the gut microbiota. Due to individual variation in the microbiota of the lower gastrointestinal tract, the results of the study may not be fully conclusive, and it is necessary to continue studies on large groups of subjects, with the additional use of questionnaires on the level of severity of symptoms associated with IBS, as well as those on mood disorders. The small number of studies on the topic addressed and their limitations related to the aforementioned individual differences in gut microbiota composition translate into a fundamental limitation of our review. The primary limitation of the study is the multitude of studies on the gut microbiota in people diagnosed with IBS, but this does not mean that they all address the issue presented in this manuscript. Many of the papers retrieved and included in the review imply a link between the microbiota, stress, and gastrointestinal complaints, but a small number are concerned with specific probiotic strains, particularly psychobiotics, and these are often validated in an animal model. We are aware that with such a large number of studies, important reports may have been omitted, but it should be noted that every effort was made to ensure that this review was conducted fairly, taking into account large, multi-centre research projects and highlighting mainstream research.

## 5. Conclusions

Functional intestinal disorders, which include irritable bowel syndrome, are associated with many symptoms that reduce quality of life. There is a correlation between the severity of symptoms and the presence of stress factors and increased emotional reactivity. In addition, the gut microbiota composition of people with irritable bowel syndrome is similar to those of people with depression. Properly planned treatment, which includes probiotic supplementation, can significantly improve the quality of life of IBS patients. The use of psychobiotics, which have been shown to decrease stress markers and reduce intestinal complaints intensified by stress, may have additional benefits and increase the effectiveness of therapy. The best-studied probiotic strain that reduces IBS symptoms and simultaneously exhibits psychobiotic effects is *Lactiplantibacillus plantarum* 299v. It is recommended to start probiotic therapy with single-strain or dual-strain formulations with proven clinical efficacy. There is a need for more studies evaluating the effects of *Lactiplantibacillus plantarum* 299v and other strains beneficial to IBS-related stress markers and emotional reactivity, conducted on people with irritable bowel syndrome, as well as studies evaluating the effects of psychobiotics on gastrointestinal symptoms.

**Author Contributions:** Conceptualization, W.G. and K.K.-K.; methodology, W.G., P.H. and K.K.-K.; investigation, W.G., P.H. and K.K.-K.; resources, W.G. and P.H.; data curation, W.G.; writing—original draft preparation, W.G. and P.H.; writing—review and editing, W.G., P.H., M.G. and K.K.-K.; visualization, W.G., P.H. and K.K.-K.; supervision, M.G. and K.K.-K.; project administration, K.K.-K.; funding acquisition, K.K.-K. All authors have read and agreed to the published version of the manuscript.

**Funding:** This research received no external funding.

**Institutional Review Board Statement:** The research complies with the provisions of the Helsinki Declaration.

**Informed Consent Statement:** Not applicable.

**Data Availability Statement:** Not applicable.

**Conflicts of Interest:** The authors declare that they have no conflict of interest.



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